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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/036,351	11/09/2001	David A. Brake	PC9898B	4450

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EXAMINER	
GRASER, JENNIFER E	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/036,351	Brake et al.
Examiner	**Art Unit**
Jennifer Graser	1645

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Prel. Amendts. A & B, 11/01 & 12/02*

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *29-38* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideratio

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *29-38* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

The Preliminary Amendments filed 11/9/01 and 2/26/02 have been entered. Claims 29-38 are currently pending and under examination.

Claim Rejections - 35 USC § 112-Deposit Requirement

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 31-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification lacks complete deposit information for the deposit of *N.caninum* strain NC-1. Because it is not clear that the properties of *N.caninum* strain NC-1 are known and publicly available or can be reproducibly isolated from nature without undue experimentation and because claims 31-33 specifically require the use of said strain, a suitable deposit for patent purposes is required. Exact replication of the strain is an unpredictable event.

If the deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of the deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under

the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the date of the deposit and the complete name and full street address of the depository is required.

If the deposits have not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR §1.801-1.809, assurances regarding availability and permanency of deposits are required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request;

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

© the deposits will be maintained in a public depository for a period of at least thirty years from the date of the deposit or for the enforceable life of the patent or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become non-viable or non-replicable.

In addition, a deposit of the biological material that is capable of self-replication either directly or indirectly must be viable at the time of the deposit and during the term of deposit. Viability may be tested by the depository. The test must conclude only that the deposited material is capable of reproduction. A viability statement for each deposit of a biological material not made under the Budapest Treaty must be filed in the application and must contain:

1)The name and address of the depository;

2)The name and address of the depositor;

3)The date of deposit;

4)The identity of the deposit and the accession number given by the depository;

5)The date of the viability test;

6)The procedures used to obtain a sample if the test is not done by the depository; and

7)A statement that the deposit is capable of reproduction.

As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the deposit was made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the cell line described in the specification as filed is the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material

described in the specification and in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR §1.801-1.809 for further information concerning deposit practice.

Claim Rejections - 35 USC § 112-Scope of Enablement

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 29-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for protecting a mammal against neosporosis, comprising administering to the mammal a vaccine comprising an immunologically effective amount of a *Neospora* homogenate as prepared in Example 1 of the specification, i.e., Neospora antigen (NSA) preparation, and a veterinarily acceptable carrier, does not reasonably provide enablement for "a method for protecting a mammal against neosporosis, comprising administering to the mammal a vaccine comprising an immunologically effective amount of a homogenate prepared from cells of *Neospora*, which homogenate is capable of inducing a protective response against neosporosis in a mammal, and a veterinarily acceptable carrier". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. .

The prior art teaches that it is extremely unpredictable to treat or prevent neosporosis in mammals. Further, the prior art specifically teaches that the use of homogenates prepared from cells of *Neospora*, as recited in the claims, can be used to induce neosporosis in mammals. Numerous prior art references teach that homogenates prepared from *Neospora* tachyzoites and cells infected with *Neospora* tachyzoites can successfully reproduce *Neospora* infection and death in mammals. See Barr et al. J.Vet Diagnosis. 1993. 6(2): 7308; Lindsay et al. Am.J.Vet Res., 1995. 56(9): 1176-1180; and Lindsay et al. J.Parasitol. 1990. 76(3): 410-413, for example. The vaccine recited in the instantly claimed methods does not distinguish over the homogenates used in these prior art references which actually induce, not protect against, neosporosis. Accordingly, the current scope of the claims is not enabled for methods of protecting against neosporosis.

However, Applicants have found that preparing homogenates from *Neospora* tachyzoites and/or cells infected with *Neospora* tachyzoites and subjecting them to protease inhibitor stocks as described in Example 1, see page 15, lines 10-29, resulted in a unique *Neospora* antigen (NSA) preparation that did not contain any viable tachyzoites. Applicants have demonstrated that the use of this preparation conferred immune protection in mammals challenged with *N.caninum*. Applicants are only enabled for this scope. The specification does not teach that any other homogenate, antigen or preparation can protect mammals against neosporosis, i.e. the use of 'an homogenate prepared from cells of *Neospora*', 'a homogenate prepared from tachyzoites', are not enabled. The distinguishing characteristics of Applicants' homogenate must be

incorporated into the claims. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims.

In summary, the prior art teaches that it is extremely unpredictable to make and use a vaccine capable of conferring protection against neosporosis. The prior art teaches that homogenates prepared from *Neospora* cells and tachyzoites actually induce disease and are, for the most part, fatal. Applicants' unique preparation which differs from that taught in the prior art refernces is what has provided the satisfactory results. Claims should be drafted to include this novel scope which would distinguish over the homogenate *Neospora* preparations recited in the prior art.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

6. Claims 29-32 and 34-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Conrad et al (WO 95/25541).

Conrad et al teach a homogenate prepared from a culture of biologically pure, isolated bovine *Neospora* tachyzoites (abstract, page 4, lines 1-13, page 8, lines 5-15, especially page 23, lines 20-22). It is specifically taught that this homogenate could be used for the prevention of Neospora infections, i.e., neosporosis. Conrad et al specifically teach administering to a mammal an effective amount of the *Neospora* vaccine in order to treat or prevent an infection caused by *Neospora*. Page 53, lines 17-20, specifically recite that "this is the first experiment to show that cattle can be protected against *Neospora* abortion by immunization with culture-derived tachyzoites of the BPA-1 *Neospora* isolate". Neosporosis is a major cause of abortion. The homogenate of Conrad et al specifically binds to the sera obtained from the cows infected with *Neospora* tachyzoites and the uninfected calves (Material and methods, and Results). The specific binding between the homogenate and the sera indicate that the homogenate contains antigens that have induce an enhanced antibody response in the tested animals. Conrad et al also teach that the homogenate from a crude extract of isolated bovine *Neospora* tachyzoites has the same antigenic components present in *Neospora caninum* NC-1. See page 33, lines 23-30 and Tables 1-2. Therefore, the homogenate prepared from a crude extract of isolated bovine *Neospora* tachyzoites BPA1 and BPA2 has equivalent antigenic components to the homogenate prepared from *Neospora caninum* NC-1 tachyzoites. Conrad further teach that the homogenate can be used with additional immunomodulatory components, such as oil-in-water emulsion, various adjuvants or cytokine (page 22, lines 1-23). The reference also teaches that the vaccine/homogenate preparation can be an attenuated *Neospora* vaccine or an antigen produced

by recombinant technology. Lastly, Conrad et al teach that the vaccine/homogenate preparation can be combined with other virus or bacterial endotoxins capable of inducing a protective response against a disease or pathological condition (page 22, lines 1-2).

Applicants' specification defines homogenate" as "a preparation prepared by homogenizing or disrupting cells of *Neospora"*. They state that "the homogenate may comprise all of the components produced by the homogenization or disruption of whole *Neospora* cells, thus representing a "whole cell" preparation. Alternatively, the homogenate may consist of a fraction of the total contents of the whole cell preparation using one or more fractionation, isolation or purification steps know in the art". See page 9, lines 11-25 of the instant specification. Accordingly, "a crude extract of Neospora tachyzoites" reads on the instant claims. See page 38, lines 34- page 39, line 5 and especially page 39, line 15-30, of Conrad which teaches that parasites were harvested, cells were disrupted, the suspension was passed through a filter to remove cellular debris and tachyzoites were pelleted by centrifugation. After removing the supernatant, the pellet was washed in buffer and resuspended in modified PBS (lines 1-30). This method clearly meets Applicants' definition of a homogenate produced by disruption of whole cells of Neospora tachyzoites. Additionally, the methods which use fractions and antigens prepared from the homogenates disclosed by Conrad also anticipate the claims because the specifications definition of 'homogenate' includes "a fraction of the total contents of the whole cell preparation using one or more fractionation, isolation or purification steps know in the art".

7. Claims 29-32 and 34-38 are rejected under 35 U.S.C. 102(e) as being anticipated by Conrad et al (5,889,166).

Conrad et al teach pharmaceutical compositions for the treatment and prevention of Neospora infections (abstract). The reference discloses that a "biologically pure bovine Neospora culture" refers to a continuous in vitro culture of bovine Neospora organisms (e.g. tachyzoites) which is substantially free of other organisms other than the host cells in which Neospora tachyzoites are grown (col. 2, lines 42-45). Vaccines may comprise a crude extract of Neospora tachyzoites (column 12, lines 51-52). The homogenate prepared from a crude extract of isolated bovine *Neospora* tachyzoites BPA1 and BPA2 has equivalent antigenic components to the homogenate prepared from *Neospora caninum* NC-1 tachyzoites. It is specifically disclosed that "cows infected using culture-derived tachyzoites mount a protective immune response and prevent transplacental infection of the fetus (col. 11, lines 60-65 and col. 28, lines 1-4). Column 11, lines 65 through column 12, lines 1-20, recite that the vaccines may comprise one or more immunomodulatory components, such as adjuvants or cytokines which include interleukin-1, 2 and gamma. The vaccines are designed to be given to cattle and other animals (col. 12, lines 39-42).

Art Made of Record:

Barta et al (Parasitol. Res. 1992. 78: 689-694).

Barta et al teach a homogenate prepared from *Neospora* tachyzoites of an NC-1 isolate (see abstract, and materials and methods). The homogenate of Barta et al. specifically binds to

the sera obtained from rabbits infected with *Neospora* tachyzoites. The reference teaches immunizing rabbits with live *Neospora* tachyzoites of an NC-1 isolate for the production of anti-*N.caninum* antibodies to be used in Western Blot analysis. However, the reference does not teach that the rabbits were protected against neosporosis, nor does it teach or suggest methods for protecting a mammal against neosporosis..

8. Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is (703) 308-4242 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (703) 308-1742. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J Graser 2/3/03

JENNIFER E. GRASER
PRIMARY EXAMINER